PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 6013-140PCT	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/CA2004/001823	International filing date *(day/month/year)* 14 October 2004 (14-10-2004)	Priority date *(day/month/year)* 14 October 2003 (14-10-2003)

International Patent Classification (IPC) or national classification and IPC
IPC: ***C07K 14/47*** (2006.01) , ***A61K 38/17*** (2006.01) , ***A61K 35/52*** (2006.01) , ***A01N 1/02*** (2006.01)

Applicant
UNIVERSITÉ LAVAL ET AL

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. [ ] *(sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      [ ] sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      [ ] sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. [ ] *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - [X] Box No. I Basis of the report
   - [ ] Box No. II Priority
   - [X] Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - [ ] Box No. IV Lack of unity of invention
   - [X] Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - [ ] Box No. VI Certain documents cited
   - [X] Box No. VII Certain defects in the international application
   - [X] Box No. VIII Certain observations on the international application

Date of submission of the demand 18 July 2005 (18-07-2005)	Date of completion of this report 28 February 2006 (28-02-2006)
Name and mailing address of the IPEA/CA Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 001(819)953-2476	Authorized officer Colleen MacFarlane (819) 997-4614

Box No. I Basis of the report

1. With regard to the **language**, this report is based on:

[X] the international application in the language in which it was filed

[ ] a translation of the international application into , which is the language of a translation furnished for the purposes of:

[ ] international search (Rules 12.3(a) and 23.1(b))

[ ] publication of the international application (Rule 12.4(a))

[ ] international preliminary examination (Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

[X] the international application as originally filed/furnished

[X] the description:

[X] pages 1-19 as originally filed/furnished

[ ] pages* received by this Authority on

[ ] pages* received by this Authority on

[X] the claims:

[X] pages 20-21 as originally filed/furnished

[ ] pages* as amended (together with any statement) under Article 19

[ ] pages* received by this Authority on

[ ] pages* received by this Authority on

[X] the drawings:

[X] pages 1/14-14/14 as originally filed/furnished

[ ] pages* received by this Authority on

[ ] pages* received by this Authority on

[ ] a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. [ ] The amendments have resulted in the cancellation of:

[ ] the description, pages

[ ] the claims, Nos.

[ ] the drawings, sheets/figs

[ ] the sequence listing *(specify):*

[ ] any table(s) related to sequence listing *(specify):*

4. [ ] This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

[ ] the description, pages

[ ] the claims, Nos.

[ ] the drawings, sheets/figs

[ ] the sequence listing *(specify):*

[ ] any table(s) related to sequence listing *(specify):*

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The question whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

[ ] the entire international application

[X] claims Nos. 1, 2, 5, 6, 11, 13, 14 and 16

because:

[ ] the said international application, or the said claims Nos.
relate to the following subject matter which does not require an international preliminary examination *(specify)*:

[X] the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 1, 2, 5, 6, 11, 13, 14, 16
are so unclear that no meaningful opinion could be formed *(specify)*:

see Supplemental Box

[X] the claims, or said claims Nos. 1, 2, 5, 6, 11, 13, 14 and 16 are so inadequately supported
by the description that no meaningful opinion could be formed *(specify)*:

see Supplemental Box

[ ] no international search report has been established for said claims Nos.

[ ] a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

[ ] furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

[ ] furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

[ ] pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b) and 13*ter*.2.

[ ] a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

[ ] the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

[X] See Supplemental Box for further details.

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	3, 4, 9, 10, 12	YES
	Claims	1, 2, 7, 8, 11, 13-16	NO
Inventive step (IS)	Claims	NONE	YES
	Claims	1-4, 7-16	NO
Industrial applicability (IA)	Claims	1-4, 7-16	YES
	Claims	NONE	NO

2. Citations and explanations (Rule 70.7)

Reference is made to the following documents:

D1: ECOYD et al. "Tyrosine phosphorylation of HSP-90 during mammalian sperm capacitation." Biology of Reproduction, December 2003, vol. 69, pages 1801-1807. (Published online before print July 30, 2003, Accession No. DOI.1095/biolreprod.103.017350)

D2: HUANG et al. "The decline of porcine sperm motility by geldanamycin, a specific inhibitor of heat-shock protein 90 (HSP90)." Theriogenology, 200, vol. 53, pages 1177-1184.

D3: HUANG et al. "Substantial decrease of heat-shock protein 90 precedes the decline of sperm motility during cooling of boar spermatozoa." Theriogenology, 1999, vol. 51, pages 1007-1016.

D4: IKAWA et al. "Calmegin is required for fertilin α/β heterodimerization and sperm fertility." Developmental Biology, 2001, vol. 240, pages 254-261.

D5: IKAWA et al. "The putative chaperone calmegin is required for sperm fertility." Nature, June 1997, vol. 387, pages 607-611.

D6: OKABE et al. "The putative chaperone calmegin and sperm fertility." from "The Male Gamete" in Basic Science to Clinical Application, pages 47-54. Editor: Claude Gagnon. Publisher: Cache River Press, Vienna, III., 1999.

NOVELTY

The problem to be solved in the instant application is the provision of polypeptides capable of binding chaperone receptors for preserving, restoring or improving the physiological properties of sperm cells in order to facilitate fertilization.

Document D1 discloses the tyrosine phosphorylation and activation of a HSP90 polypeptide during capacitation and implicates it, as a representative chaperone polypeptide in the process by which sperm gain the ability to fertilize the oocyte. Accordingly, then, D1 anticipates claims 1, 2, 7, 8, 11 and 13-16 contravening Article 33(2) PCT.

continued in Supplemental Box

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

There is no description of Figures 13 and 14 in the "Brief Description of Drawings" section in the description as is required under Rule 5.1(iv) PCT.

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are

The expressions, "a polypeptide capable of binding a chaperone receptor" (claims 1, 11, 13 and 16) and "a molecule capable of binding sperm cell chaperone" (claim 2), are functional definitions and do not clearly define the chemical structures and thus are not in compliance with Article 6 (PCT). Similarly, the terms, "matrix protein" (claims 2, 5 and 14) and "analogs or fragments thereof" (claims 2 and 14), are not clearly defined in terms of their specific chemical structures, also contravening Article 6 (PCT). In addition, these expressions and terms are so broad as to encompass compounds not contemplated by the Applicant and do not find adequate support in the description and thus the description is not in compliance with Article 5 (PCT).

The expression, "at least one" (claim 2), is indefinite and does not comply with Article 6 (PCT) since it is unclear whether the claims encompasses a mixture/composition of polypeptides or whether the claim encompasses a singular polypeptide as suggested by parent claim 1.

Similarly, claims 9 and 10 do not comply with Article 6 (PCT) as it is unclear as to whether these claims encompass compositions of a polypeptide in a "diluent medium" or whether the claims encompass the polypeptide itself as suggested by parent claim1.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box III

The expressions, "a polypeptide capable of binding a chaperone receptor" (claims 1, 11, 13 and 16) and "a molecule capable of binding sperm cell chaperone" (claim 2), are functional definitions and do not clearly define the chemical structures and thus are not in compliance with Article 6 (PCT). Similarly, the terms, "matrix protein" (claims 2, 5, and 14) and "analogs or fragments thereof" (claims 2 and 14), are not clearly defined in terms of their specific chemical structures, also contravening Article 6 (PCT). In addition, these expressions and terms are so broad as to encompass compounds not contemplated by the Applciant and which do not find adequate support in the description and thus the description is not in compliance with Article 5 (PCT). Consequently, no opinion has been rendered for claims 1, 2, 5, 6, 11, 13, 14 and 16 insofar as they relate to said terms and expressions.

Continuation of Box V:

Huang et al. report the decline in porcine sperm motility with exposure to geldanamycin, a specific HSP90 inhibitor, in D2 and that a substantial decrease in HSP90 precedes the decline of sperm motility in cooled boar spermatozoa in D3, implicating HSP90 as crucial to sperm motility. Claim 1, 2, 7, 8, 11 and 13-16 are therefore considered to be anticipated by D2 or D3 under Article 33(2) PCT.

Documents D4, D5 and D6 disclose the chaperone, calmegin, in relation to sperm fertility. With their disclosure in D5 that loss of endoplasmic reticulum calmegin results in the production of sterile sperm which do not bind to the zona pellicuda in calmegin -/- mice, Ikawa et al. further disclose in D4 that calmegin -/- sperm were defective in their migration into the oviduct and in adhesion to the egg plasma membrane. Taken together, D4 and D5 clearly demonstrate calmegin is required for sperm migration, zona pellucida adhesion and egg plasma membrane adhesion. D6 also discloses calmegin's crucial role in male fertility. Accordingly, documents D4, D5 and D6 are considered as novelty-destroying for claims 1, 2, 7, 8, 11 and 13-16 (Article 33(2)).

D1-D6 do not specifically disclose GRP 78, Sec A, Sec B, Sec Y or GroEL in relation to the physiological properties of sperm, nor do they disclose specific concentrations, compositions or methods using the chaperone polypeptides to improve the physiological properties of sperm. Claims 3, 4, 9, 10 and 12 are therefore considered novel under Article 33(2) PCT.

INVENTIVE STEP

Although the prior art does not specifically disclose a role for GRP 78 (claim 4) or Sec A, Sec B, Sec Y or GroEL (claim 2) or HSP60 (claim 3) in male fertility, because of their structural and functional similarities to the other chaperone polypeptides discussed in D1-D6, particularly the heat shock proteins, it would be within the competence of a skilled technician to conclude that they would have a similar effect on sperm physiological properties. Similarly, an inventive step is not required to simply determine effective concentrations of the chaperone polypeptides (claims 9 and 10) or basic compositions comprising the chaperones (claim 12). Thus, an inventive step cannot be acknowledged under Article 33(3) PCT for the subject matter of claims 3, 4, 9, 10 or 12 in view of D1-D6.

INDUSTRIAL APPLICABILITY

Claims 1-4 and 7-16 appear to define subject matter that has industrial applicability under Article 33(4) PCT based on the putative ability of chaperone polypeptides to improve physiological properties of sperm to facilitate fertilization.